CASE REPORT

Embolia Cutis Medicamentosa: A Forgotten Entity

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Abstract

Introduction: Embolia cutis medicamentosa [Nicolau syndrome (NS) or livedoid dermatitis] is a rare adverse reaction developed cutaneously after an intramuscular (IM) or intra-arterial injection (Inj).

Case discussion: A 65-year-old female came with complaints of a painful lesion over the left gluteus region and gave a history of diclofenac sodium IM Inj at that site 1 day prior at a local clinic for recurrent oral ulcers. A well-defined violaceous necrotic indurated plaque of 10 × 7 cm with crusting and surrounding erythema and tenderness was noted over the left gluteus. Clinically a diagnosis of necrotizing fasciitis, livedoid vasculitis, and NS was made. Routine investigations showed eosinophilia, thrombocytosis, and reduced serum calcium.

Histopathology showed neutrophilic perivascular and periadnexal infiltration with focal denudation of the epidermis suggestive of NS.

For treatment of surgical debridement, Inj dexamethasone 4 mg intravenous (IV) for 3 days and pentoxifylline 400 mg orally three times a day (PO t.i.d) was started along with platelet-rich fibrin matrix wound dressing.

Conclusion: NS is an uncommon iatrogenic complication and is a forgotten entity; physicians and healthcare workers should be kept informed of this rare entity and should be trained to administer Injs properly.

Keywords: Diclofenac sodium, Embolia cutis medicamentosa, Nicolau syndrome.

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Introduction

Embolia cutis medicamentosa, also called NS or livedoid dermatitis was initially described in 1924, by Freudenthal when an intragluteal IM Inj of bismuth salts was administered to treat syphilis.[1] Intramuscular, subcutaneous,[2,3] IV,[4] and intra-articular[5] Injs have also been reported to cause this syndrome. Etiopathogenesis remains unknown.

Intense pain immediately postinjection period and purplish discoloration of the skin is characteristic of the disease. It can turn gangrenous and can even cause renal failure and rarely even death.[6]

Nonspecific signs and symptoms can pose a dilemma to the clinician and are often misdiagnosed. This case report emphasizes the need to shed light on this condition and the need to practise due care during any parenteral Inj administrations by dermatologists and cosmetic surgeons.

Case Description

A 65-year-old Indian female presented with bluish discoloration of the skin over the left hip region for 2 days associated with aching pain. She gave a history of diclofenac sodium Inj at the site a day prior at the local clinic for recurrent oral ulcers. There was no history of trauma or use of any topical or systemic medication.

On clinical examination, a large well-defined violaceous necrotic indurated plaque of about 10 × 7 cm with crusting and surrounding erythema and tenderness was noted over the superomedial aspect of the left gluteus region (Fig. 1). Based on the given history and clinical features, a differential diagnosis of necrotizing fasciitis, livedoid vasculitis, and NS was considered.

Routine investigations showed eosinophilia, thrombocytosis, and reduced serum calcium. Two 3.5 mm skin biopsies were taken, one from the border of the healthy lesion, and another from the unhealthy necrosed skin over the left gluteus.

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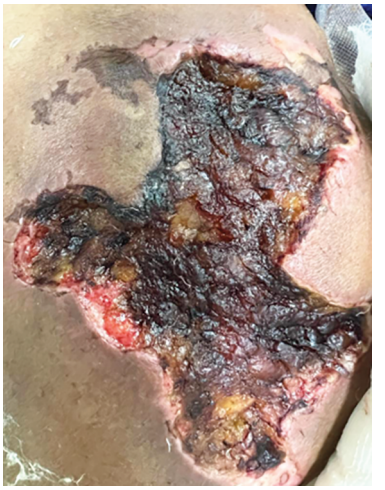

Fig. 1: Clinical image of the lesion

Histopathology from the healthy tissue showed mild hyperkeratosis and irregular acanthosis of the epidermis. Dermis shows perivascular and periadnexal inflammatory infiltrate, predominantly neutrophils which were nonspecific. Histopathology of the necrotized tissue showed focal denunciation of the epidermis with focal necrosis of the epidermis. Dermis shows hyalinization, thickened vessel walls, and lumen occluded by a thrombus suggestive of NS (Fig. 2).

For treatment of surgical debridement, Inj. dexamethasone 4 mg IV for 3 days and pentoxifylline 400 mg PO t.i.d was started. The wound dressing with the platelet-rich fibrin matrix derived from the patient's serum was done (Figs 3 to 5).

Discussion

Nicolau syndrome (NS) is an iatrogenic condition that was initially only thought to occur after an IM Inj. There are multiple theories regarding this pathophysiology. One of which was that NS is likely to occur due to thrombosis of a vessel and cause necrosis of the subcutaneous tissue and muscle when an IM administration hits the arterial wall or lumen. Stimulation of the sympathetic nerves, embolic occlusion, blockade of prostaglandin synthesis, physical obstruction, and inflammation of the blood vessels have also been considered in its pathogenesis.[7] Multiple drugs such as nonsteroidal anti-inflammatory drugs, penicillin, local anesthetics, and corticosteroids are some of the drugs implicated to cause NS. Phenobarbital, gentamicin, chlorpromazine, diphtheria-pertussis-tetanus vaccine, dexamethasone, and lidocaine and diphenhydramine, when administered intramuscularly, has also led to NS.[7,8]

Al-Sheeb et al,[9] recently reported NS after an endodontic treatment with calcium hydroxide. Clinically, there is a sudden onset of symptoms. There will be skin discoloration, intense pain, and inflammation. A hemorrhagic patch with necrosis at the Inj site and livedoid dermatitis usually follow.

Hypoesthesia and paraplegia are the transitional neurological complications seen in one-third of the patients.[10] There are few reports of patients developing hyperkalemia, compartment syndrome of the limbs, renal failure, and even death.[11] Embolism could be causative of paralysis of limbs. Embolus of the internal iliac artery and even the vertebral canal can occur when there is an embolus in the vessel of the gluteal muscle. Paralysis and disturbance of the peripheral nerve are caused by this arterial stenosis.[12] Presentations of this syndrome can vary and the criteria to diagnose this is not definite.

The most common differential diagnosis for this is necrotizing fasciitis and livedoid vasculitis. However, the recent history of Inj is a diagnostic clue to diagnose NS.

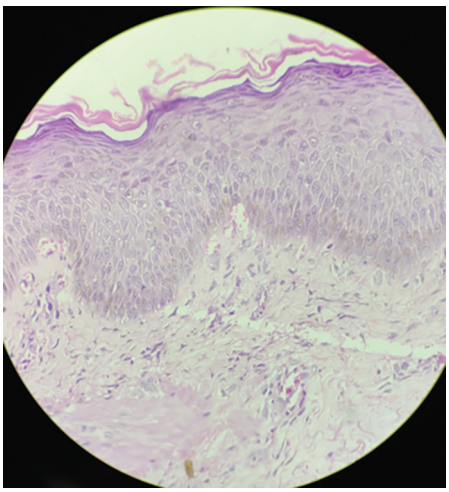

Fig. 2: Histopathology of the necrotized tissue

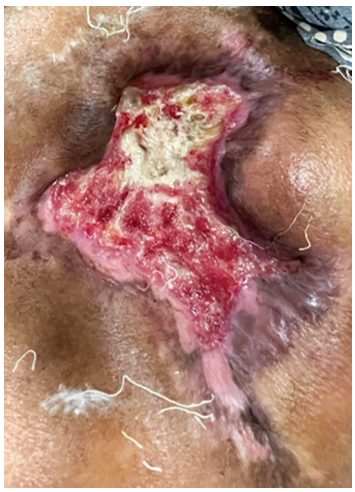

Fig. 4: A 1 month posttreatment of the lesion

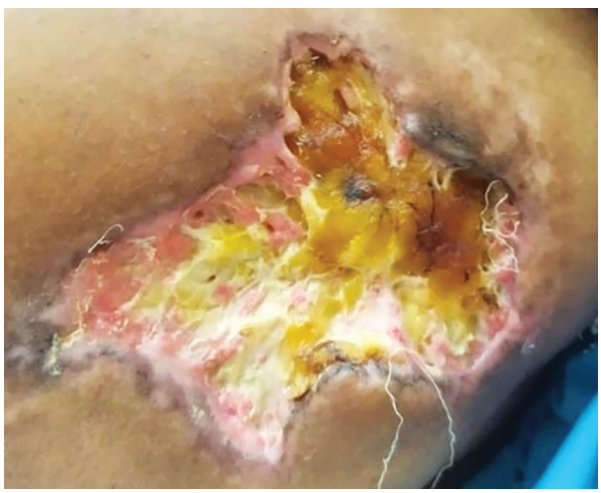

Fig. 3: The 7 days posttreatment of the lesion

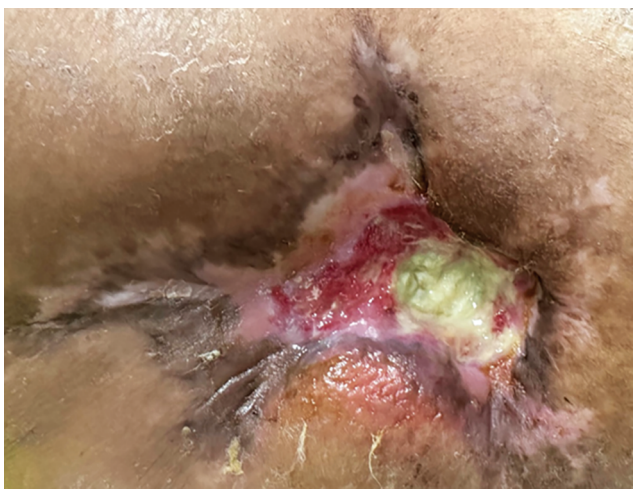

Fig. 5: A 2 months posttreatment of the lesion

So far, the treatment of NS has no consensus. Phasic treatments range from surgical debridement to medication depending on the extent of the necrotic lesion. Anticoagulant agents and systemic steroids are usually started due to the hypothesis of a vascular origin.[13]

Hyperbaric oxygen treatment with heparin and pentoxifylline is given if microarterial thrombi involvement is considered.[14] Heparin 5000–10000 U two times a day given subcutaneous and betamethasone diphosphate 24 mg/d IV infusion are the other reported treatment options.

Dexamethasone 32 mg IV or methylprednisolone 1g IV every day for 3 days has also been given. Surgical debridement of the affected region, and once the healthy granulation is attained split-thickness graft and if extensive damage reconstructive surgery can also be performed.[13]

In accordance with the published literature, surgical debridement, Inj. dexamethasone 4 mg IV for 3 days and pentoxifylline 400 mg PO t.i.d was started. The wound was dressed with a platelet-rich fibrin matrix.

Conclusion

Nicolau syndrome (NS) is an uncommon iatrogenic complication and is a forgotten entity which that physicians and healthcare workers should be aware of. There are severe complications of NS and it can be avoided just by following the correct method of Inj.

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